Claims:

A method for preventing or treating anthrax infections by inhibiting
Anthrax Lethal Factor activity comprising
administering a compound of the formula:

wherein U and V are, independently, C, N, or C(CH₃), L1 is a linker and R1, R2, R3 and R4 are each independently selected substituent groups, as follows:

R1 is Z(CHR5)_nY where n is 0 to 4,

Z is a bond, S, CO, O, SO, SO₂, NH, NR11, SO₂NR11, NR11SO₂, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 1,2-cyclohexylidene;

Y is a group known to bind to zinc, including CONR11OH, COOH, SH, ArSH, NHCOCH₂SH, 2-hydroxybenzoate (linked at the 3,4,5, or 6-position), 2-hydroxypyridinecarboxylate (linked at the 3,4,5, or 6-position, with the ring nitrogen at any unsubstituted position), CF₂P=O(OH)₂, C(CH₃)=NOCH₂COOH, C(CH₂OH)=NOCH₂COOH, NHCO(CHR11)_mSH (where m = 1 to 4), PO(OH)₂, PO(R11)OH, SO₂NR11OH, or NH(OH)COR11, or is derivatized to form a prodrug that is capable of undergoing conversion to a zinc-binding moiety,

R5 and R11 are, independently, H, CH₃, amino, hydroxy, alkoxy, alkylthio, alkyl (C2-C10), branched alkyl (C3-C10), alkylthio (C1-C7), alkylthioalkyl (C2-C8), arylthio,

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alkylamino(C1-C7), amino, arylamino, aryl, heteroaryl, arylalkyl, heterarylalkyl, arylalkynyl, or heterarylalkynyl,

and where R1 can be further substituted with one or more of the following: NH₂, OH, halogen, alkyl, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, CN, NO₂, NR6R7 where R6 and R7 are H or alkyl and optionally form a ring, or R5 can form a ring with R2 or with R11;

R2 is H, isobutyl, n-butyl, pentyl, methyl, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl, cycloalkylmethyl (C3-C9 cycle), Ar(CH₂)n (where n is 0 to 4, Ar is phenyl, aryl, heteroaryl), phenethyl, arylalkenyl, heterarylalkenyl, arylalkynyl, heterarylalkynyl, alkenyl (C2-C8), alkynyl (C2-C8), pentafluorophenoxyethyl, pentafluorophenylmethyl, cycloalkenyl (C4-C10), alkylthio, arylthio, alkylamino, arylamino, aryl, dichlorophenyl, or R2 can form a ring with R5, R11, L1, or R3, and R2, R5 and R11 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, SO₂alkyl (C1-C4), CONH₂, CONHOH, C(NH)NH₂, CN, NO₂, C(NH)NHOH, NHC(NH)NH₂, or NR6R7 where R6 and R7 are H or alkyl and can form a ring;

R3 is H, phenethyl, alkyl (C1-C10), branched alkyl (C1-C10), aryl, phenyl substituted with aryl or heteroaryl at the 2-, 3-, or 4-positions, benzyloxy, pyrrolyl substituted with 1-2 aryl groups, 2-aryl-1,3,4 thiadiazolyl, heteroaryl (including thiophenyl), -L2Ar where Ar includes 1-naphthyl, 2-naphthyl, 4-phenylphenyl, 5-(2-thienyl)-2-thienyl, 4-(3'-methoxyphenyl)phenyl, 4-(4'-methoxyphenyl)phenyl, 3-indolyl, phenyl, t-butyl, indolyl 3-phenylphenyl, indolyl, 2,3-dimethyl-5-indolyl, benzothiophenyl, 4-(1,2,3-thiadiazol-4-yl)phenyl, 4-(2-thienyl)phenyl, 5-(2-pyridyl)-2-thienyl, 1-(2-napthyl)vinylaminoalkyl, N-hydroxybenzamidin-4-yl, 2-methylcarbazol-3-yl, 2-ethylcarbazol-3-yl, aryl or heteroaryl and L2 is a linker chosen from the following, in both orientations: bond, CH₂, (CH₂)₂, CH₂NHCH₂, CH₂CONHCH₂, CH₂CNHCH₂, CH₂CONHCH₂, CH₂CH₂CNHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂

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(CHR9)sX(CHR9)t where s + t = 0 to 8, X is O, S, CO, SO, SO₂, NH, CONH, NHCO, SO₂NH, NHSO₂ or NR9 and R9 is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), acyl, alkyl thio, amino, alkyl amino, or dialkylamino, and R9 also includes N-linked heterocycles such as piperidine, pyrroline, (1,2,3,4-)tetahydrobetacarbolin-2yl, R15 is H, alkyl (C1-C4), branched alkyl (C3-C5), or cycloalkyl(C3-C5), carbon-carbon single bonds in R8 can optionally be substituted with double or triple bonds, and where R3 can form a ring with R2, L1, or R4, or R3, R9 and R15 are further substituted with one or more of the following NH₂, OH, halogen, N(CH₃)₂ alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, CN, NO₂, C(NH)NHOH, NHC(NH)NH₂, aryloxy, trifluoromethylphenyloxy, carboxyalkyl (C2-C8), (Carboxyphenyl)methylthio, carboxyalkylthio (C2-C8), carboxyphenyl, NR6R7 where R6 and R7 are H or alkyl or can form a ring;

R4 is H, alkyl (C1-C10), branched alkyl (C1-C10), arylalkyl, heteroarylalkyl, CONR10R16 where R10 is H, methyl, alkyl (C2-C10), branched alkyl (C3-C10), benzyl, phenethyl, arylalkyl, heteroarylalkyl, alkanoyl (C2-C8), branched alkanoyl, aroyl (C6-C12), heteroaroyl (C2-C10), isopropyl,CONR16R12; and where R12 and R16 are, independently, H, methyl, alkyl, benzyl, 2-phenylethyl, 2-indanyl, 2-morpholinylethyl, (2,6)-dimethoxylbenzyl, dimethylaminoethyl, (2-pyridyl)methyl, 2-(2-pyridyl)ethyl, 4-carboxybenzyl, 1-phenylethyl, CH(CONH₂)CH₂C₆H₅, CH(CONH₂)CH₂CH(CH₃)₂, CH(CONH₂)CH(CH₃)CH₂CH₃, CH(CONH₂)CHCH₃ CH(CONH₂)CH₂C₆H₅, CH(CONHCH₂CH₃)CH₂Cyclohexyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, aminoalkyl, hydroxyalkyl, (trifluoromethylphenoxy)phenyl. NR16R12 can optionally form an N-linked monocyclic or bicyclic heterocyclic ring, including but not limited to 1,2-dihydroisoindole, octahydroisoindole, morpholine, piperidine, piperazine, N-alkyl piperazine (C1-C4), homopiperazine, 3-pyrroline, pyrrolidine, tetrahydroisoquinoline, octahydropyrrolo[3,4-C]pyrrole, L-proline, L-proline dimethylamide, D-proline, D-proline dimethylamide, and thiazolidine, or

R4 can form a ring with L1 or R3, and R4, R6, R7, R10, R11, R12 and R16 can be further substituted, independently, with 1 to 3 of the following substitutents: NH₂, OH, F, Cl, Br, methyl, alkyl, aryl, cycloalkyl (C3-C6), heterocycloalkyl, heteroaryl, CF₃,

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CF₃O, CF₃S, CF3, aryloxy, trifluoromethylphenoxy, alkoxy, alkylthio, CONH₂, CN, NO₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl, or can form a ring; and

L1 is a linker including the following, in either orientation: single bond, double bond, CONH, NHCO, N(CH₃)CO, CON(CH₃), CH₂NH, NHCH₂, CH=CH,C(NH₂)=N, N=C(NH₂), arylene (linked 1,2-; 1,3-; or 1,4), heteroarylene (linked 1,2-; 1,3-; or 1,4), ethynyl, CH=CF, CF=CH, CF=CF, CH₂CH₂, C(CH₃)=CH, CH=C(CH₃), SO₂NH, SO₂, COCH₂, CH₂CO, CNOHCH₂, CH₂CNOH, C(CF₃)=CH, CH=C(CF₃), SO₂CH₂, CH₂SO₂, SOCH₂, CH₂SO, CH₂CHOH, CHOHCH₂, lower cycloalkyl (C3-C6), or CHOHCHOH, or where L1 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl and optionally form a ring.

2. A pharmaceutical composition useful for preventing or treating anthrax infections by inhibiting Anthrax Lethal Factor activity comprising a compound of the formula:

wherein U and V are, independently, C, N, or C(CH₃), L1 is a linker and R1, R2, R3 and R4 are each independently selected substituent groups, as follows:

R1 is Z(CHR5)_nY where n is 0 to 4,

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Z is a bond, S, CO, O, SO, SO₂, NH, NR11, SO₂NR11, NR11SO₂, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 1,2-cyclohexylidene;

Y is a group known to bind to zinc, including CONR11OH, COOH, SH, ArSH, NHCOCH₂SH, 2-hydroxybenzoate (linked at the 3,4,5, or 6-position), 2-hydroxypyridinecarboxylate (linked at the 3,4,5, or 6-position, with the ring nitrogen at any unsubstituted position), CF₂P=O(OH)₂, C(CH₃)=NOCH₂COOH, C(CH₂OH)=NOCH₂COOH, NHCO(CHR11)_mSH (where m = 1 to 4), PO(OH)₂, PO(R11)OH, SO₂NR11OH, or NH(OH)COR11, or is derivatized to form a prodrug that is capable of undergoing conversion to a zinc-binding moiety,

R5 and R11 are, independently, H, CH₃, amino, hydroxy, alkoxy, alkylthio, alkyl (C2-C10), branched alkyl (C3-C10), alkylthio (C1-C7), alkylthioalkyl (C2-C8), arylthio, alkylamino(C1-C7), amino, arylamino, aryl, heteroaryl, arylalkyl, heterarylalkyl, arylalkenyl, heterarylalkenyl, arylalkynyl, or heterarylalkynyl,

and where R1 can be further substituted with one or more of the following: NH₂, OH, halogen, alkyl, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, CN, NO₂, NR6R7 where R6 and R7 are H or alkyl and optionally form a ring, or R5 can form a ring with R2 or with R11;

R2 is H, isobutyl, n-butyl, pentyl, methyl, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl, cycloalkylmethyl (C3-C9 cycle), Ar(CH₂)n (where n is 0 to 4, Ar is phenyl, aryl, heteroaryl), phenethyl, arylalkenyl, heterarylalkenyl, arylalkynyl, heterarylalkynyl, alkenyl (C2-C8), alkynyl (C2-C8), pentafluorophenoxyethyl, pentafluorophenylmethyl, cycloalkenyl (C4-C10), alkylthio, arylthio, alkylamino, arylamino, aryl, dichlorophenyl, or R2 can form a ring with R5, R11, L1, or R3, and R2, R5 and R11 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, SO₂alkyl (C1-C4), CONH₂, CONHOH, C(NH)NH₂, CN, NO₂, C(NH)NHOH, NHC(NH)NH₂, or NR6R7 where R6 and R7 are H or alkyl and can form a ring;

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R3 is H, phenethyl, alkyl (C1-C10), branched alkyl (C1-C10), aryl, phenyl substituted with aryl or heteroaryl at the 2-, 3-, or 4-positions, benzyloxy, pyrrolyl substituted with 1-2 aryl groups, 2-aryl-1,3,4 thiadiazolyl, heteroaryl (including thiophenyl), -L2Ar where Ar includes 1-naphthyl, 2-naphthyl, 4-phenylphenyl, 5-(2-thienyl)-2-thienyl, 4-(3'methoxyphenyl)phenyl, 4-(4'-methoxyphenyl)phenyl, 3-indolyl, phenyl, t-butyl, indolyl 3-phenylphenyl, indolyl, 2,3-dimethyl-5-indolyl, benzothiophenyl, 4-(1,2,3-thiadiazol-4yl)phenyl, 4-(2-thienyl)phenyl, 5-(2-pyridyl)-2-thienyl, 1-(2-napthyl)vinylaminoalkyl, Nhydroxybenzamidin-4-yl, 2-methylcarbazol-3-yl, 2-ethylcarbazol-3-yl, aryl or heteroaryl and L2 is a linker chosen from the following, in both orientations: bond, CH₂, (CH₂)₂, CH₂NHCH₂, CH₂CONHCH₂, CH₂CH₂CONHCH₂CH₂, 1,1 vinylidene, 1,2-vinylidene, CO, CH₂CH₂NHCH₂, CH₂CH₂NHCH₂, CH₂NHCH₂CH₂, (CH₂)q where q = 3 to 7, (CHR9)r where r = 1 to 7 and R9 is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), alkyl thio, amino, alkyl amino, dialkylamino, (CHR9)sX(CHR9)t where s + t = 0 to 8, X is O, S, CO, SO, SO₂, NH, CONH, NHCO, SO₂NH, NHSO₂ or NR9 and R9 is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkyl (C4-C14), acyl, alkyl thio, amino, alkyl amino, or dialkylamino, and R9 also includes N-linked heterocycles such as piperidine, pyrroline, (1,2,3,4-)tetahydrobetacarbolin-2yl, R15 is H, alkyl (C1-C4), branched alkyl (C3-C5), or cycloalkyl(C3-C5), carbon-carbon single bonds in R8 can optionally be substituted with double or triple bonds, and where R3 can form a ring with R2, L1, or R4, or R3, R9 and R15 are further substituted with one or more of the following NH2, OH, halogen, N(CH3)2, alkyl, CF3, CF3O, CF3S, alkoxy, alkylthio, CONH2, CONHOH, C(NH)NH2, CN, NO2, C(NH)NHOH, NHC(NH)NH2, aryloxy, trifluoromethylphenyloxy, carboxyalkyl (C2-C8), (Carboxyphenyl)methylthio, carboxyalkylthio (C2-C8), carboxyphenyl, NR6R7 where R6 and R7 are H or alkyl or can form a ring;

R4 is H, alkyl (C1-C10), branched alkyl (C1-C10), arylalkyl, heteroarylalkyl, CONR10R16 where R10 is H, methyl, alkyl (C2-C10), branched alkyl (C3-C10), benzyl, phenethyl, arylalkyl, heteroarylalkyl, alkanoyl (C2-C8), branched alkanoyl, aroyl (C6-

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C12), heteroaroyl (C2-C10), isopropyl,CONR16R12; and where R12 and R16 are, independently, H, methyl, alkyl, benzyl, 2-phenylethyl, 2-indanyl, 2-morpholinylethyl, (2,6)-dimethoxylbenzyl, dimethylaminoethyl, (2-pyridyl)methyl, 2-(2-pyridyl)ethyl, 4-carboxybenzyl, 1-phenylethyl, CH(CONH₂)CH₂C₆H₅, CH(CONH₂)CH₂CH(CH₃)₂, CH(CONH₂)CH(CH₃)CH₂CH₃, CH(CONH₂)CHCH₃ CH(CONH₂)CH₂C₆H₅, CH(CONHCH₂CH₂OCH₃)CH₂cyclohexyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, aminoalkyl, hydroxyalkyl, (trifluoromethylphenoxy)phenyl. NR16R12 can optionally form an N-linked monocyclic or bicyclic heterocyclic ring, including but not limited to 1,2-dihydroisoindole, octahydroisoindole, morpholine, piperidine, piperazine, N-alkyl piperazine (C1-C4), homopiperazine, 3-pyrroline, pyrrolidine, tetrahydroisoquinoline, octahydropyrrolo[3,4-C]pyrrole, L-proline, L-proline dimethylamide, D-proline, D-proline dimethylamide, and thiazolidine, or

R4 can form a ring with L1 or R3, and R4, R6, R7, R10, R11, R12 and R16 can be further substituted, independently, with 1 to 3 of the following substitutents: NH₂, OH, F, Cl, Br, methyl, alkyl, aryl, cycloalkyl (C3-C6), heterocycloalkyl, heteroaryl, CF₃, CF₃O, CF₃S, CF3, aryloxy, trifluoromethylphenoxy, alkoxy, alkylthio, CONH₂, CN, NO₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl, or can form a ring; and

L1 is a linker including the following, in either orientation: single bond, double bond, CONH, NHCO, N(CH₃)CO, CON(CH₃), CH₂NH, NHCH₂, CH=CH,C(NH₂)=N, N=C(NH₂), arylene (linked 1,2-; 1,3-; or 1,4), heteroarylene (linked 1,2-; 1,3-; or 1,4), ethynyl, CH=CF, CF=CH, CF=CF, CH₂CH₂, C(CH₃)=CH, CH=C(CH₃), SO₂NH, SO₂, COCH₂, CH₂CO, CNOHCH₂, CH₂CNOH, C(CF₃)=CH, CH=C(CF₃), SO₂CH₂, CH₂SO₂, SOCH₂, CH₂SO, CH₂CHOH, CHOHCH₂, lower cycloalkyl (C3-C6), or CHOHCHOH, or where L1 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl and optionally form a ring, together with a pharmaceutically acceptible carrier.